Obsessive Compulsive Drinking Scale

Directions: The questions below ask you about your drinking alcohol and your attempts to control your drinking **in the last week**. Please circle the number next to the statement that best applies to you.

1. How much of your time when you're not drinking is occupied by ideas, thoughts, impulses or images related to drinking?

   (0) None
   (1) Less than 1 hour a day
   (2) 1-3 hours a day
   (3) 4-8 hours a day
   (4) Greater than 8 hours a day

2. How frequently do these thoughts occur?

   (0) Never
   (1) No more than 8 times a day
   (2) More than 8 times a day but most hours of the day are free of those thoughts
   (3) More than 8 times a day and during most hours of the day
   (4) Thoughts are too numerous to count and an hour rarely passes without several such thoughts occurring

   Insert the Higher Score of Question 1 or 2 here ____

3. How much do these ideas, thoughts, impulses or images related to drinking interfere with your social or work (or role) functioning? Is there anything you don't or can't do because of them? (If you are not currently working, how much of your performance would be affected if you were working?)

   (0) Thoughts of drinking never interfere – I can function normally.
   (1) Thoughts of drinking slightly interfere with my social or occupational activities, but my overall performance is not impaired
   (2) Thoughts of drinking definitely interfere with my social or occupational performance, but I can still manage.
   (3) Thoughts of drinking cause substantial impairment in my social or occupational performance.
   (4) Thoughts of drinking interfere completely with my social or work performance.

4. How much distress or disturbance do these ideas, thoughts, impulses, or images related to drinking cause you when you're not drinking?

   (0) None
   (1) Mild, infrequent and not too disturbing
   (2) Moderate, frequent and disturbing, but still manageable
   (3) Severe, very frequent and very disturbing
   (4) Extreme, nearly constant, and disabling distress

5. How much of an effort do you make to resist these thoughts or try to disregard or turn your attention away from these thoughts as they enter your mind when you're not drinking? (Rate your effort made to resist these thoughts, not your success or failure in actually controlling them.)

   (0) My thoughts are so minimal, I don't need to actively resist. If I have thoughts, I make an effort to *always* resist.
   (1) I try to resist most of the time.
   (2) I make some effort to resist.
   (3) I give in to all such thoughts without attempting to control them, but I do so with some reluctance.
   (4) I completely and willingly give in to all such thoughts.

6. How successful are you in stopping or diverting these thoughts when you're not drinking?

   (0) I am completely successful in stopping or diverting such thoughts.
   (1) I am usually able to stop or divert such thoughts with some effort and concentration.
   (2) I am sometimes able to stop or divert such thoughts.
   (3) I am rarely successful in stopping such thoughts and can only divert such thoughts with difficulty.
   (4) I am rarely able to divert such thoughts even momentarily.

7. How many drinks do you drink each day?

   (0) None
   (1) Less than 1 drink per day
   (2) 1-2 drinks per day
   (3) 3-7 drinks per day
   (5) 8 or more drinks per day

8. How many days each week do you drink?

   (0) None
   (1) No more than 1 day per week
   (2) 2-3 days per week
   (3) 4-5 days per week
   (4) 6-7 days per week

Insert the Higher Score of Question 7 or 8 here ___

9. How much does your drinking interfere with your work functioning? Is there anything that you don't or can't do because of your drinking? (If you are not currently working, how much of your performance would be affected if you were working?)

(0) Drinking never interferes – I can function normally
(1) Drinking slightly interferes with my occupational activities, but my overall performance is not impaired.
(2) Drinking definitely interferes with my occupational activities, but I can still manage.
(3) Drinking causes substantial impairment in my occupational performance.
(4) Drinking problems interfere completely with my work performance.

10. How much does your drinking interfere with your social functioning? Is there anything that you don't or can't do because of your drinking?

(0) Drinking never interferes – I can function normally.
(1) Drinking slightly interferes with my social activities, but my overall performance is not impaired.
(2) Drinking definitely interferes with my social performance.
(3) Drinking causes substantial impairment in my social performance.
(4) Drinking problems interfere completely with my social performance .

Insert the Higher Score of Questions 9 or 10 here ____

11. If you were prevented from drinking alcohol when you desired a drink, how anxious or upset would you become?

(0) I would not experience any anxiety or irritation.
(1) I would become only slightly anxious or irritated.
(2) The anxiety or irritation would mount but remain manageable.
(3) I would experience a prominent and very disturbing increase in anxiety or irritation.
(4) I would experience incapacitating anxiety or irritation.

12. How much of an effort do you make to resist consumption of alcoholic beverages? (Only <u>rate your effort to resist</u>, not your success or failure in actually controlling the drinking).

(0) My drinking is so minimal, I don't need to actively resist. If I drink, I make an effort to always resist.
(1) I try to resist most of the time.
(2) I make some effort to resist.
(3) I give in to almost all drinking without attempting to control it, but I do so with some reluctance.
(4) I completely and willingly give in to all drinking.

13. How strong is the drive to consume alcoholic beverages?

(0) No drive
(1) Some pressure to drink
(2) Strong pressure to drink
(3) Very strong drive to drink
(4) The drive to drink is completely involuntary and overpowering.

14. How much control do you have over the drinking?

(0) I have complete control.
(1) I am usually able to exercise voluntary control over it.
(2) I can control it only with difficulty.
(3) I must drink and can only delay drinking with difficulty.
(4) I am rarely able to delay drinking even momentarily.

Insert the higher score of Question 13 or 14 here _____

Total ____ *(sum all items adjusting for combined items)*

Obsessive Subscale _____ *(Sum items 1 to 6 adjusting for combined items)*

Compulsive Subscale _____ *(Sum items 7 to 14 adjusting for combined items)*

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REVIEW

A comparison of rating scales for the alcohol-withdrawal syndrome

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ABSTRACT

— This paper reviews the literature on the use of rating scales within the treatment of the alcohol-withdrawal syndrome. A computer-assisted literature search identified trials of therapy for and rating scales used in alcohol-withdrawal states. Eighteen rating scales were identified. There is a wide variation in symptom items included in these scales. Scales also vary in their length and ease of application. We conclude that it is important to use validated and reliable assessment scales in research if proper comparisons of treatments for the alcohol-withdrawal syndrome are to be made.

INTRODUCTION

One of the major problems for researchers and reviewers of treatment methods for alcohol withdrawal is the lack of a widely used, reliable and validated rating scale (Williams and McBride, 1998). Several different scales have been used within this field of research. Comparison difficulties are further exacerbated by the failure to use strict, comparable inclusion and exclusion criteria for study and control groups. Use of recognized diagnostic criteria, such as those laid out in ICD-10 (World Health Organization, 1992) or DSM-IV (American Psychiatric Association, 1994), with standardized ratings of dependency would aid comparison of the study populations.

An ideal rating scale in this area of research should: (i) aid the diagnosis of the withdrawal syndrome; (ii) indicate when drug therapy is required; (iii) alert staff to the development of serious withdrawal

symptoms requiring more intensive medical input; (iv) reveal when medication can be discontinued and the patient safely discharged. Such a tool would be useful in research and would facilitate comparisons between studies on existing and newer medications. Study groups could be compared both in terms of symptom presentation and severity. This would then allow treatment response to be accurately and consistently measured. In clinical practice, such a tool would allow clinicians to assess and predict those who require pharmacological treatment on the basis of symptom severity and to titrate the dose required.

The aims of the present work were to identify rating scales used in the assessment of acute alcohol withdrawal described in the literature and then to compare their content and ease of application. Information with regard to reliability and validity was also sought.

METHODS

A computer literature search and reference search of review articles traced papers published in the English language between 1973 and 1999 on pharmacological treatments of alcohol-withdrawal states. The year 1973 was selected as the earliest date because it was the year Gross *et al.* (1973) published the Total Severity Assessment (TSA) and the shortened version, the Selected Severity Assessment (SSA). Of the 38 papers reviewed, 23 described rating scales in sufficient detail for their content to be analysed. Only those using a standardized system of scoring specific symptoms of withdrawal, and producing an overall measure of severity, were included. Four used a previously published scale so that, in total, 18 different scales were included.

RESULTS

Table 1 shows the symptoms and scoring systems used by all the studies. This reveals the lack of consensus between existing scales as to which symptoms constitute the most significant indicators of the alcohol-withdrawal syndrome. No single symptom was included in all the scales analysed and scales differed in the numbers of items included. A total of 30 symptoms and signs were described.

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Table 1. Number of points given to each symptom on rating scales

Anxiety was included in most scales (McGrath, 1975; Bjorkqvist *et al.*, 1976; Poutanen, 1979; Borg and Weinholt, 1980, 1982; Ritola and Malinen, 1981; Shaw, 1981; Agricola *et al.*, 1982; Flygenring *et al.*, 1984; Kraus *et al.*, 1985; Brunning *et al.*, 1986; Saunders, 1987; Gallimberti *et al.*, 1989; Benzer, 1990; Wetterling *et al.*, 1997). Loss of co-ordination (one scale: Bjorkqvist *et al.*, 1976), flushing (one scale: Shaw, 1981) and dizziness (two scales: Bjorkqvist *et al.*, 1976; Poutanen, 1979) were the least frequently used criteria. Blood pressure, pulse and temperature were often measured as part of the overall assessment, but were included in only five scales (Gross *et al.*, 1973; Kraus *et al.*, 1985; Saunders, 1987; Benzer, 1990; Wetterling *et al.*, 1997). The scoring systems ranged from

'Yes/No' for the presence of symptoms to 9-point scales. Scales 1–8 did not specify scoring criteria in the paper, whereas scales 9–16 did.

Table 2 illustrates the wide variations in the weightings given to different symptom groups by the rating scales. Figures given are the percentage contribution of each group of symptoms to the total scale scores. The seven groupings were those of affect, gastrointestinal (GI) disturbance, autonomic nervous system (ANS) disturbance, neurological disturbance, sleep, psychotic features and seizures. This comparison emphasizes the disparity in the weighting of items in the scales. Reasons for the particular make-up of the scales concerned were not published in the original descriptions. Some of the scales appear to be biased towards the known actions of the drugs under investigation. For example the scale which gives the highest weighting to autonomic symptoms, such as hypertension and raised pulse rate (Scale 11, Kraus *et al.*, 1985), was used in investigating the beta blocker, atenolol. The scale that gave the highest weighting to seizures was used in investigating carbamazepine (Agricola *et al.*, 1982).

View this table: Table 2. Percentage score of different symptom groups
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The most widely used scales, and those from which several other scales have been derived, are the Total Severity Assessment (Gross *et al.*, 1973) and the clinical Institute Withdrawal Assessment Scale for Alcohol (Shaw *et al.*, 1981). Both are well validated and will now be described in more detail.

Total Severity Assessment scale

The TSA scale was developed by Gross *et al.* (1973) in an attempt to improve differentiation of degrees of severity in alcohol-withdrawal states and facilitate the quantification of the withdrawal syndrome. Gross *et al.* began by reviewing 10 previously published scales utilized in a variety of treatment studies. These varied from those that simply recorded the presence or absence of symptoms, to those that rated severity. Gross *et al.* (1973) considered them all to be inadequate and produced their own prototype TSA. The scale contains 30 variables which are rated on an 8-point scale. Zero indicates the absence of a symptom, whilst 7 indicates the maximum severity. The 30-item scale was intended as a research tool and a shorter 11-item scale, the SSA, was produced for clinical use.

Reliability of the instruments was assessed by randomly selecting 18 in-patients in 'acute withdrawal' who were then assessed by two nurses, individually, each day. The different nurses visited the patients $2^1/2$ h apart. Correlation coefficients were then calculated. Of the 30 items, eight, including three SSA items, were not evaluated. Six of the 22 items rated (including two SSA) did not show statistically significant correlation between the two assessors' scores. This left only 16 of the 30 items in the TSA (six of 11 SSA) with statistically significant correlations, suggesting that they might be reliable measures of withdrawal severity. Gross *et al.* (1973) explained the low level of reliability by the inherent fluctuation in symptom severity in what is an acute organic brain syndrome. Subsequent trials revealed the TSA to be valid when compared to global rating scales, but the extensive training of evaluators

required to achieve reliability limited widespread use.

Clinical Institute Withdrawal Assessment (CIWA) scale

The CIWA scale for alcohol was developed from the SSA, to enable use at more frequent intervals during the day. This resulted in a 15-item scale, which retained just seven of the 11 SSA items. Inter-rater reliability was demonstrated by comparing assessments made by seven trained nurses on three video cases. Validity was considered by comparison of scores on CIWA rated by nurses, with a 3-point global rating of severity of withdrawal made by a physician at the initial assessment (Shaw, 1981⊞). Further trials have shown a modified CIWA to minimize under- and over-dosing with benzodiazepines in the treatment of alcohol

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Table 1. Number of points given to each symptom on rating scales

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	Borg and Weinhoff (1980, 1982) (*n* = 24)	Bjorkvist *et al.* (1976) (*n* = 105)	McGrath (1975) (*n* = 100)	Flygenring *et al.* (1984) (*n* = 72)	Gallimberti *et al.* (1989) (*n* = 11)	Ritola and Malinen (1981) (*n* = 68)	Poutanen (1979) (*n* = 106)	Agricol *et al.* (1982) (*n* = 55
Anxiety	6	3	5	5	4	4	3	3
Restlessness	6	3	5	5	4		3	3
Irritability		3		5		4	3	3
Depression	6	3		5	4	4	3	3
Anorexia		3					3	3
Nausea	6	3			4		3	3
Vomiting							3	3
GI disturbance		3	5			4	3	3
Temperature								
Sweating	6	3	5	5	4		3	3
Flushing								
Tachycardia								
Palpitations		3				4	3	3
Hypertension								
Headache	6	3					3	3
Tremor	6	3		5	4		3	3
Impaired co-ordination			5					
Altered consciousness			5					3
Concentration			5					
Dizziness		3					3	3

Neurological				6		
Insomnia	3			4	3	3
Sleep disturbance	3				3	3
Hallucinations	3	5		4	3	3
Visual disturbance						
Auditory disturbance						
Tactile disturbance						
Delusions		5				3

*Paper simply describes the scale and does not test its use on a study sample.

GI = gastrointestinal.

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Trauma and substance cue reactivity in individuals with comorbid posttraumatic stress disorder and cocaine or alcohol dependence

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Abstract

Although the high comorbidity of posttraumatic stress disorder (PTSD) and substance use disorders has been firmly established, no laboratory-based studies have been conducted to examine relationships between the two disorders. Using cue reactivity methodology, this study examined the impact of personalized trauma-image cues and *in vivo* drug cues on drug-related responding (e.g. craving) in individuals with PTSD and either crack cocaine (CD) or alcohol dependence (AD). CD and AD groups displayed reactivity to both trauma and drug cues when compared to neutral cues, including increased craving. However, the AD group was more reactive than the CD group to both classes of cues. The CD participants were more reactive to trauma-image cues if drug-related material was included in the image while the AD participants were reactive to the trauma cues regardless of drug-related content. It is

hypothesized that PTSD-related negative emotion may play a relatively more important role in the maintenance of AD when compared to CD. Evidence that substance dependent individuals with PTSD report increased substance craving in response to trauma memories is offered as a potential contributing factor in the poorer substance abuse treatment outcomes previously documented in this comorbid population.

Author Keywords: Drug dependence; Posttraumatic stress disorder; Comorbidity; Cue reactivity; Emotion; Imagery

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Article Outline

1. Introduction

Recently, numerous studies have shown that induced negative emotion increases craving in alcohol dependent individuals (e.g. Cooney; Litt and Rubonis). For example, Rubonis and colleagues (1994) found that personalized alcohol-related negative mood induction prior to alcohol cue exposure increased reactivity to an alcohol cue in alcohol dependent men and women. Cooney et al. (1997) found that personalized negative emotional cues unrelated to alcohol use (i.e. guided imagery) increased alcohol craving in alcohol dependent males. Moreover, craving elicited by negative emotional cues combined with *in vivo* alcohol cues were significant predictors of time to relapse in these men. These studies have used a laboratory-based research methodology known as cue reactivity to elucidate the role that emotion may play in the maintenance of, and relapse to, substance use. Cue reactivity refers to a phenomenon in which individuals with a history of drug dependence exhibit verbal, physiological, and behavioral responses to cues associated with their preferred substance of abuse. These associated cues may be emotional, cognitive, or physical in nature. The responses elicited by the cues differ from verbal, physiological, and behavioral responses to non-substance-related control cues (see Drummond et al., 1995).

Although the role of negative emotion has been studied in substances other than alcohol (e.g. Childress; Coffey and Maude), very little experimental work has been conducted on cocaine dependence. Recently, however, the effects of psychological stress on cocaine craving have been examined using a laboratory-based paradigm (Sinha et al., 1999). Neutral and personalized stress imagery tasks were presented to 10 cocaine abusers followed by ratings of cocaine craving and anxiety. Participants reported higher cocaine craving and anxiety following the personalized imagery stress task than following the neutral image. In contrast, Cannon et al. (1992), using a correlational design, found that substance use during negative emotional states was reported more often by alcohol dependent males than by cocaine dependent males. In addition, within males dependent on both cocaine and alcohol, alcohol use was more likely than cocaine use during periods of negative emotion. Thus, the literature appears to be equivocal regarding the relation of negative emotion and drug-related responses in cocaine dependence. Therefore a goal of the present study was to examine the role of negative emotion in cocaine dependence.

The reviewed literature suggests that emotion may play an important modulatory role in substance use disorders (SUD). This would suggest that persons with a SUD and a comorbid disorder with strong emotional features may be particularly reactive to emotional and substance cues. A comorbid population that has received growing attention and has strong emotional features is SUD-posttraumatic stress disorder (PTSD) comorbid individuals (Grice; Najavits; Brown and Back). In addition to the high co-occurrence of SUD and PTSD, there is evidence that PTSD may be uniquely deleterious to SUD treatment outcome. For example, comparisons between SUD-PTSD comorbid patients and patients with either a SUD alone or a SUD and a comorbid psychiatric condition other than PTSD reveal that SUD–PTSD patients have a higher addiction severity, are more likely to have comorbid psychiatric disorders, have poorer substance use treatment outcome, and have a higher number of inpatient admissions (Brady; Najavits; Brown and Ouimette).

One possible explanation for the high prevalence of PTSD within SUD populations and this

group's poorer treatment outcome is the presence of PTSD-related negative emotion. Intrusive symptoms in the form of memories, dreams, or flashbacks are one of the core diagnostic symptom clusters of PTSD according to the Diagnostic and Statistical Manual (DSM-IV; American Psychiatric Association, 1994). To meet diagnostic criteria, the intrusion symptoms must be significantly distressing. Therefore, for individuals with SUD–PTSD, negative emotional states resulting from intrusive symptoms, as well as other symptoms of PTSD, are relatively common and disturbing experiences and may adversely affect their substance abuse treatment.

The present study was designed to investigate whether cues that produce traumatic memories and images would elicit substance craving and other related responses in SUD–PTSD comorbid individuals. Individuals with PTSD and either cocaine or alcohol dependence were presented with personalized trauma-image cues and neutral-image cues followed by drug-related or neutral cues. Following presentation of the cues, participants rated their emotional and drug-related responses elicited by the imagery scripts and the drug and neutral cues. We predicted trauma cues and drug cues would each increase drug craving and related responses over responses elicited by the neutral cues. Due to the nature of victimization in SUD populations, we also wished to determine if the presence of drug-related verbal content within personalized imagery scripts would modulate cue reactivity. In addition, there is some data suggesting that negative emotion may have a differential effect depending on the individual's preferred substance (Cannon et al., 1992), therefore, a secondary goal of the study was to compare the pattern of cue reactivity in cocaine and alcohol dependent participants. To date, no study that we are aware of has directly examined CD and AD subjects in parallel cue reactivity paradigms.

2. Methods

2.1. Study overview

Cocaine dependent (CD) and alcohol dependent (AD) individuals with PTSD participated in a laboratory-based cue reactivity protocol that consisted of two sessions. The first session was an assessment session to determine study eligibility. During the second session, participants were administered a two-phase cue reactivity protocol. The first phase was the presentation of an imagery cue delivered via headphones. The cue was either a narrative description of the participant's worst crime-related traumatic event (e.g. rape by a stranger) or a narrative of a neutral cue (e.g. brushing one's teeth). Immediately following the imagery phase, the second phase involved the presentation of an *in vivo*cue, either cues related to the participant's preferred substance (e.g. Jack Daniel's whisky) or neutral cues (e.g. wood chips). Although the imagery cue always preceded the *in vivo* cue, the two cues in each phase were fully counterbalanced. Following each cue combination, participants rated both cue types.

2.2. Participants

Thirty individuals meeting current diagnostic criteria for PTSD and CD and 45 individuals meeting diagnostic criteria for PTSD and AD (DSM-IV; APA, 1994) were recruited from inpatient and outpatient substance use treatment programs at the Medical University of South Carolina (a tertiary care teaching hospital) and local treatment facilities in the Charleston, SC area. All participants met PTSD diagnostic criteria as a result of a criminal victimization experience (e.g. direct physical or sexual assault either as a child or as an adult) and reported use of their preferred substance within 60 days of the laboratory session. Individuals were

excluded if they met diagnostic criteria for a psychotic disorder, were currently experiencing a manic episode, or were experiencing severe depression. In addition, individuals were excluded if they were engaged in PTSD-related treatment. Participants were not excluded if they met dependence criteria for a substance other than cocaine or alcohol. In addition, while all CD participants reported their preferred substance was cocaine, they were not excluded if they also met diagnostic criteria for AD. Likewise, all AD participants reported that their preferred substance was alcohol but were not excluded if they met diagnostic criteria for CD. All CD participants were dependent on crack cocaine. Demographic information on the CD and AD groups is provided in Table 1. All participants were treated in accordance with the 'Ethical Principles of Psychologists and Code of Conduct' (American Psychological Association, 1992) and all participants were financially compensated for their participation.

Table 1. Mean (S.D.) participant characteristics

 (18K)

2.3. Instruments

2.3.1. Diagnostic measures

2.3.1.1. Structured Clinical Interview for the DSM-IV (SCID-IV):

Psychiatric suitability for study inclusion and substance use disorder was determined using the SCID-IV (First et al., 1996). The substance use section of an earlier version of the SCID-IV (SCID-III-R; Spitzer and Williams, 1986) has demonstrated good validity (Kranzler et al., 1996) and has shown high interrater reliability for substance use disorders (Skre et al., 1991).

2.3.1.2. National Women's Study (NWS) PTSD Module and the Clinician Administered PTSD scale:

Information regarding participants' trauma history was collected with the NWS PTSD Module (Kilpatrick et al., 1989), a structured interview modified from the Diagnostic Interview Schedule used in the National Vietnam Veterans Readjustment Study (NVVRS; Kulka et al., 1990). DSM-IV criterion was used to identify reported traumas that satisfied PTSD Criterion A, the necessary stressor criterion for PTSD. For study inclusion, however, it was required that participants report at least one crime-related Criterion A event that significantly contributed to the diagnosis of PTSD. Crime-related events were defined as a direct physical or sexual assault that occurred in either childhood or adulthood. Concurrent validity with the SCID–PTSD module was good and reliability was also acceptable (Resnick et al., 1993). The clinician administered PTSD scale (CAPS; Blake et al., 1995), a psychometrically sound structured clinical interview, was used as the diagnostic tool for current PTSD.

2.3.2. Self-report ratings of trauma, craving, drug dependence, and mood

To measure trauma-related symptoms, the Impact of Event Scale-Revised (IES–R; Weiss and Marmar, 1997) was used. Items on the IES-R represent the three DSM-IV PTSD symptom

clusters of intrusion, avoidance, and arousal. Craving was measured using two scales. The Cocaine Craving Questionnaire-Now (CCQ-Now; Tiffany et al., 1993) assesses current craving for cocaine and was administered to the CD group while the Alcohol Craving Questionnaire (ACQ-Now; Singleton et al., 1995) assesses current craving for alcohol and was administered to the AD group. Likewise, drug dependence was measured using two scales. To assess alcohol-related problems and symptoms, the Short Michigan Alcoholism Screening Test (SMAST; Selzer et al., 1975) was administered to the AD group while the Drug Abuse Screening Test (DAST; Skinner, 1982) was used to assess drug involvement. Finally, the Beck Depression Inventory (BDI; Beck et al., 1961) was administered to all participants to assess for depressive symptoms.

2.4. Imagery cues

Two classes of imagery cues were employed in the study: a personalized trauma script and a neutral script. The personalized trauma cue was a 50 s audiotaped narrative presented over headphones. Information for the trauma script, which vividly described the participants' worst crime-related trauma from the first person perspective, was collected during the assessment session. Participants' selected their neutral imagery script from a pool of five standard 50 s neutral scripts that have been used in previous research and contain descriptions of multiple sensory dimensions to assist in the production of vivid images (Coffey and Drobes). During the assessment session, participants read and rated the five scripts on valence (i.e. pleasantness) and arousal dimensions. For each participant, the script rated closest to neutral on both dimensions was selected for presentation.

2.5. *In vivo* cues

Two classes of *in vivo* cues were employed in the study: drug cues and neutral cues. For the AD group, the drug cue was the sight and smell of the participants' preferred alcoholic beverage. The beverage was presented in a clear glass container directly under the participants' nose on an adjustable-height table in his or her typical manner of consumption (e.g. Jack Daniels over ice). The bottle of the participants' preferred brand of alcohol also was presented with the label facing the participant. Since all CD participants used crack cocaine, the drug cue for the CD group was the sight of a small, clear bag of simulated crack cocaine, the participants' preferred style of crack pipe, and a lighter presented on a small tray. To further promote drug craving, participants were told that the simulated crack cocaine was authentic cocaine.

The neutral cue for both the AD and CD groups were wood chips presented on a small tray. However, to control for olfactory alcohol cues presented to the AD group, the wood chips for the AD group were aromatic cedar chips, while for the CD group the woods chips were less fragrant pine chips.

2.6. Ratings of the imagery and *in vivo* cues

Self-Assessment Manikin (SAM; Bradley and Hodes) was used to rate the imagery and *in vivo* cues on the dimensions of valence, arousal, and dominance using a graphical computer version of SAM. This task involves changing the appearance of a computerized cartoon figure to correspond to each dimension of emotion being rated (e.g. SAM's valence rating ranges from a figure with a large smile to a figure with a pronounced frown, arousal ratings range from a figure that appears drowsy to an agitated figure, and the dominance ratings

range from a very small figure to a very large figure). This method of rating subjective emotions has been used by researchers investigating emotional responses to stimuli (Hodes; Miller and Bradley).

Visual analog scale ratings (VAS) were used by participants to rate both the *in vivo* cues and the imagery cues. Participants rated their level of craving in response to the stimuli, their desire to consume their preferred substance when presented with the stimuli (i.e. approach), their desire to avoid consuming their preferred substance when presented with the stimuli (i.e. avoidance) and the vividness of the imagery cues. All four VAS ratings consisted of 21-point line ratings on a computer monitor with `not at all' and `very much so' serving as anchors for the scales. Both VAS and SAM ratings were recorded automatically and stored directly on a computer for later analysis.

2.7. Procedure

All participants were screened either in person or over the telephone for the possible presence of either AD or CD and the presence of a PTSD Criterion A event. Based on positive findings in the initial screening, potential participants were scheduled for an assessment session

2.7.1. Assessment session

The study design and goals were described to all participants and informed consent was obtained. In addition to the standard study description, CD participants were told that they would view authentic crack cocaine during the experimental session. The mild deception was employed to increase the likelihood that the procedure would produce elevations in craving for the CD group.

To establish study eligibility, an experienced research assistant interviewed participants. The SCID-IV, NWS PTSD module, and CAPS were used to (a) establish current AD or CD; (b) assess for exclusionary psychiatric diagnoses; (c) assess participants' victimization history and to establish the presence of the necessary Criterion A stressor for PTSD; and (d) establish a current diagnosis of PTSD. It was not required that the diagnosis of PTSD be associated with a singular crime-related event because most participants had experienced multiple vicitimizations. However, it was required that the participant relate at least 75% of reported PTSD symptoms to one or more crime-related event that satisfied Criterion A for PTSD.

If participants met study inclusion and exclusion criteria following the structured interviews, they were asked to describe their worst crime-related trauma. Participants were told that the information they provided would be included in a 50 s audiotaped narrative that would be presented to them over headphones during the laboratory session. Participants were encouraged to include multiple sensory dimensions in their victimization description, including physical sensations, thoughts, emotions, olfactory cues, visual details, and events that they avoided due to the trauma or elicit memories of the trauma. Finally, AD and CD participants completed the SMAST and DAST, respectively, and all participants completed the IES-R. Upon completion of the self-report measures, the laboratory session was scheduled to take place within one week of the assessment session.

Participants were required to maintain abstinence from alcohol and illicit drugs for 4 days

prior to the laboratory session. Participants who either reported drug or alcohol use in the 4 days preceding the laboratory session or tested positive for the metabolites of cocaine, opioids, amphetamines, or marijuana, were rescheduled. In addition, subjects were asked to abstain from nicotine for 2 h and caffeine for 4 h prior to the laboratory session.

2.7.2. Laboratory session

All laboratory sessions were scheduled to begin between 14:00 and 16:00 h to control for diurnal variations that could effect cue reactivity. Upon arrival to the laboratory, participants' compliance with the substance use restrictions was assessed. A urine drug screen (UDS; Roche Diagnostic Systems, Inc., Somerville, NJ) was conducted at the beginning of the laboratory session to test for recent consumption of THC, cocaine, opiates, and amphetamines. To assess recent alcohol intoxication, expired air samples were analyzed (Alco-sensor IV, Intoximeters, Inc., St. Louis, MO) prior to the laboratory session. In addition, nicotine and caffeine use was assessed by participants' self-report. If substance screens were negative, the AD and CD participants completed the ACQ or the CCQ, respectively.

Upon completion of the craving questionnaire, participants were escorted to an acoustically insulated subject room where they were seated in a comfortable chair. Several electrodes were attached to measure physiological responses. The physiological measures are part of a larger project and will be reported elsewhere.

Four image-*in vivo* cue combinations were presented to all participants in a counterbalanced fashion (i.e. trauma imagery cue followed by a drug cue, TD; neutral imagery cue followed by a drug cue, ND; trauma imagery cue followed by a neutral cue, TN; and neutral imagery cue followed by a neutral cue, NN). The presentation of the four image–*in vivo* cue combinations followed the presentation of an NN practice trial in which participants were led through the following procedure. Participants were told that when the experimenter left the room they were to close their eyes and that an audiotaped narrative would be played over their headphones. Participants were informed that following the end of the narrative they should continue to image the scene as vividly as possible. Moreover, participants were instructed to experience the emotions elicited by the scene and to imagine the physical sensations described in the scene. After responding to participants' questions, the experimenter left the subject room and started an audiotaped narrative. Following the 50 s script presentation, participants continued to actively imagine the scene for an additional 30 s. At the end of the 30 s active imagery period, an experimenter entered the subject room and placed an *in vivo* cue on the table in front of the participant and then exited the room. A tone signaled the participant to open his or her eyes and look at the cue while continuing to image the scene previously described. Participants observed the cue for 2 min. Another tone then signaled the participant to turn to an adjacent computer monitor and first rate the *in vivo* cue and then to rate the imagery cue. Using a computer joystick, participants rated the cues in three ways: (1) for the ratings of craving, approach, and avoidance, cues were rated by moving a vertical line along a 21-point computerized VAS and pressing a button on the joystick to register their response, (2) for the ratings of valence, arousal, and dominance, by manipulating a computerized manikin figure (i.e. SAM) via a joystick to reflect the participants' emotional state when presented with each type of cue, and (3) each image was rated for it's subjective vividness on a 21-point computerized VAS. After the participant rated both the *in vivo* cue and the imagery cue, participants were queried for their understanding of the task and, if needed, task clarification was provided. The TD, ND, TN, and NN cue combinations were then presented in counterbalanced fashion in the manner

described above.

At the completion of the laboratory protocol, participants were fully debriefed and a final craving rating was obtained. The final craving rating was obtained to assure the safety of the participants upon dismissal. In addition, CD participants were informed that the crack cocaine cue was not authentic crack cocaine. In the absence of elevations in drug craving, participants were paid and thanked for their participation. If significant drug craving remained after the debriefing, an experienced clinical psychologist assisted participants in reducing their craving to baseline levels.

2.8. Statistical analysis

To test for differences between demographic variables, categorical data were analyzed using Chi-square tests of independence while continuous data were analyzed using one-way analysis of variance (ANOVA). Due to significant demographic differences between the AD and CD participants, the effects of gender, age, and race were examined to assess if potential rating dissimilarities could be attributed to demographic differences between the two groups. Stepwise linear regression and repeated measure ANOVA was used to assess whether gender, age, and race predicted the VAS and SAM ratings above and beyond substance group membership (i.e. cocaine or alcohol dependent). Repeated measures ANOVAs were used to examine differences between cocaine versus alcohol dependent participants, and as a function of (a) imagery cue type, and (b) *in vivo* cue type. These effects were assessed separately for each of the four VAS and each of the three SAM ratings. All simple effects and interactions were investigated with Tukey's HSD post hoc tests. As a secondary analysis, ANOVA was also used to assess the impact of drug-related verbal material contained within the trauma imagery scripts and was used to examine group differences on measures of drug dependence, craving, and trauma symptomatology. Linear regression was used to assess if baseline substance craving was associated with differential experimentally induced craving. For all ANOVAs, a Bonferroni adjustment was employed to reduce familywise Type I error. Familywise Type I error was reduced for each cue rating (i.e. craving, approach, avoidance, arousal, valence, and dominance) by dividing alpha (α=0.05) by the number ANOVAs conducted on the measures (4). These procedures lead to an adjusted alpha level of 0.013 for each of the in-session dependent measures except vividness. Two ANOVAs were performed on the vividness ratings, therefore, an adjusted alpha level of 0.025 was employed for that rating.

3. Results

3.1. Demographic data

Significant demographic differences were found between the CD and AD groups. The AD group was significantly older than the CD group, F (1, 74)=7.17, P<0.009, gender was not equally distributed across groups, χ^2 (1)=12.94, P<0.001 (more females were included in the CD group when compared to the AD group), and the racial makeup of the two groups differed significantly, χ^2 (2)=15.06, P<0.001 (more Caucasians were included in the AD group when compared to the CD group). Stepwise linear regression was used to assess whether the variables of age, gender, and race offered unique contributions to the prediction of the VAS and SAM ratings over the prediction provided by drug group membership (i.e. cocaine or alcohol groups). Analysis indicated that these variables did not predict SAM or

VAS ratings over the prediction provided by group membership. As a result, subsequent analyses examining the differences between the CD and AD groups do not include the variables of age, race, or gender. The CD and AD groups did not differ on PTSD symptomatology or depressive symptoms nor did the two groups differ on self-reported smoking status or days since their last use of their preferred substance.

3.2. Ratings of the imagery cues

Separate repeated measures ANOVAs were conducted on each of the SAM and VAS ratings. Means and standard deviations for the ratings are presented in Table 2 while corresponding *F*-values are presented in Table 3.

Table 2. Mean (S.D.) of the CD and AD groups' VAS and SAM ratings of the imagery and *in vivo* cues during each of the four trials

 (27K)

The four trials are: trauma-image cue–*in vivo* drug CUE=TD; trauma-image cue–*in vivo* neutral CUE=TN; neutral-image cue–*in vivo* drug CUE=ND; neutral-image cue–*in vivo* neutral CUE=NN.

Table 3. *F*-values for the ratings of the imagery and *in vivo* cues

 (12K)

After correcting for multiple comparisons, the significant level for all of the ratings was α=0.013, except for the vividness rating (α=0.025). * $P \leq 0.013$; ** $P \leq 0.001$.

3.2.1. Craving and approach

For the VAS craving and approach measures, significant main effects were found for substance with the AD group reporting significantly higher craving and approach ratings than the CD group. Significant main effects were also found for trial type, however, the Substance X Trial Type interactions did not reach significance. Post hoc analysis of the trial types revealed that the TD and TN trials produced higher craving and approach ratings than the ND or the NN trials (all *P*'s<0.003). Baseline craving (i.e. reported craving prior to the experimental manipulation), as measured by the CCQ for the CD participants and the ACQ for the AD participants, was not associated with the level of craving elicited by the imagery cues.

3.2.2. Avoidance

For the VAS rating of avoidance, a significant main effect was found for substance with the AD group reporting lower avoidance ratings than the CD group. The main effect for trial type and the Substance X Trial Type interaction did not reach significance. Differences between the AD and CD groups on the three measures of drug craving are presented in Fig. 1.

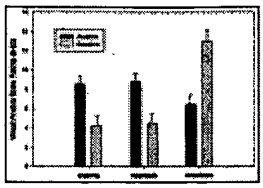
(9K)

Fig. 1. Visual Analog Scale (0–20) craving, approach, and avoidance ratings of the imagery cues. The error bars represent the standard error.

3.2.3. Arousal

For the SAM rating of arousal, a significant main effect was found for substance with the AD group reporting significantly higher arousal ratings than the CD group. A significant main effect was also found for trial type, however, the Substance X Trial Type interaction did not reach significance. Post hoc analysis of the trial types revealed that the participants reported significantly higher arousal in response to the TD and TN trials when compared to either the ND or the NN trial (all P's<0.001).

3.2.4. Valence

A significant main effect for trial type was revealed, although the main effect for substance and the Substance X Trial Type interaction did not reach significance. The TD and TN trials were rated as less pleasant than either the ND or the NN trial (all P's<0.001).

3.2.5. Dominance

For the dominance rating, a significant main effect was found for trial type and a significant Substance X Trial Type interaction was also revealed. Analysis of the Substance X Trial Type interaction revealed that for the CD group, the TD and TN trials elicited lower dominance ratings (i.e. a diminished feeling of control) than their own ND and NN trials or the ND and NN trials of the AD group (P<0.05). In addition, the TD and TN trials elicited greater dominance ratings (i.e. an enhanced feeling of control) for the CD group than for the AD group (P<0.05). For the AD group, the TD and TN trials elicited lower dominance ratings than their own ND and NN trials (P<0.05).

3.2.6. Vividness

A significant main effect was found for trial type although the main effect for substance and the Substance X Trial Type interaction did not reach significance. The personalized trauma scripts (TD and TN trials) were rated as more vivid than the standard neutral script used in the ND or NN trials (all P's<0.005).

3.3. Ratings of the *in vivo* cues

As for the analysis of the imagery cues, separate repeated measures ANOVAs were conducted on each of the SAM and VAS ratings of the *in vivo* cues. Means and standard deviations for the ratings are presented in Table 2.

3.3.1. Craving and approach

For the VAS craving and approach measures, significant main effects were found for substance with the AD group reporting significantly higher craving and approach ratings than the CD group. Significant main effects were also found for trial type, however, the Substance X Trial Type interaction did not reach significance after correcting for multiple comparisons. Analysis of the trial types found that the TD and ND trials produced higher approach ratings than the TN (each at $P<0.001$) or the NN trials (each at $P<0.001$). Baseline craving, as measured by the CCQ for the CD participants and the ACQ for the AD participants, was not associated with the level of craving elicited by the *in vivo* cues.

3.3.2. Avoidance

For avoidance, only a significant main effect was found for substance with the AD group reporting lower avoidance ratings than the CD group.

3.3.3. Arousal

For the SAM rating of arousal, a significant main effect was found for substance with the AD group reporting significantly higher arousal ratings than the CD group. A significant main effect was also found for trial type, however, the Substance X Trial Type interaction did not reach significance. Post hoc analysis of the trial types revealed that the participants reported significantly higher arousal in response to the TD and ND trials when compared to either the TN or the NN trials (all P's<0.001).

3.3.4. Valence

A significant main effect for trial type was revealed although the main effect for substance and the Substance X Trial Type interaction did not reach significance. The TD trial was rated as less pleasant than the NN trial ($P<0.001$) and the ND trial was rated as less pleasant than the TN trial ($P<0.001$).

3.3.5. Dominance

For the SAM dominance rating, a significant main effect was found for substance with AD group reporting significantly higher dominance ratings than the CD group. A significant main effect was also found for trial type, however, the Substance X Trial Type interaction did not reach significance. Analysis of the trial types found that the TD trial produced higher dominance ratings than the TN ($P<0.043$) or the NN trials ($P<0.001$) and the ND trial produced higher dominance ratings than the NN trial ($P<0.001$).

3.4. Impact of drug-related content in personalized trauma scripts on cue reactivity

To assess the impact of drug content in the trauma-related scripts on cue reactivity, both the AD and CD groups were dichotomized by the drug content of their personalized trauma scripts. Examples of drug content within a personalized trauma script included sexual assaults by an intoxicated perpetrator, physical assaults during a drug purchase, and assaults while the victim was intoxicated. Scripts with drug content were classified Drug+, while scripts without drug content were classified Drug-. The Drug+ and Drug- groups did not differ on age, gender, race, education, marital status, or income for either the CD or AD groups. Due to the striking differences in cue reactivity between the CD and AD groups, the

influence of the drug content in the trauma scripts on cue reactivity was analyzed separately for the two substance groups. Trial type differences are not reported to eliminate redundancy with the primary analyses.

3.4.1. Ratings of the imagery cues

For the CD group rating the imagery cues, a significant main effect for script content (i.e. Drug+ or Drug-) was found for craving, $F(1, 28)=5.74$, $P<0.023$, and approach, $F(1, 28)=6.27$, $P<0.018$. A nonsignificant trend was found for avoidance, $F(1, 28)=2.97$, $P<0.096$. More specifically, the CD Drug+ group reported higher craving and approach in response to the imagery cues than did the CD Drug- group and there was a tendency for the CD Drug+ group to provide higher avoidance ratings than the CD Drug- group. No significant Trial Type X Script Content interactions were found for the ratings of the imagery cues. In contrast to the CD group, no significant script content main effects or Trial Type X Script Content interactions were revealed on any of the imagery cue ratings for the AD group.

3.4.2. Ratings of the *in vivo* cues

For the CD group rating the *in vivo* cues, a significant main effect for script content was revealed for craving, $F(1, 28)=6.26$, $P<0.018$, approach, $F(1, 28)=6.18$, $P<0.019$, and valence, $F(1, 28)=7.22$, $P<0.012$. Cues that followed Drug+ scripts elicited higher craving and approach, yet elicited less positive emotional ratings. No significant Trial Type X Script Content interactions were found for the ratings of the *in vivo* cues. As seen in the AD group's ratings of the imagery cues, no significant main effects for script content was found for the AD group's rating of the *in vivo* cues.

To assess whether trauma-related or drug-related symptoms could account for ratings differences between the CD Drug+ and CD Drug- groups, groups were compared on the DAST, the CCQ, and the IES-R. No significant group differences were found on these measures.

4. Discussion

The present study presented personalized trauma and neutral imagery cues and *in vivo* drug and neutral cues to individuals comorbid for PTSD and either cocaine dependence or alcohol dependence. Subjective reactions to the imagery and *in vivo* cues were assessed on the following dimensions: drug craving, approach, avoidance, arousal, valence, and dominance. Consistent with the extant literature, CD and AD participants reported increased drug craving and other drug-relevant responses when presented with drug-related cues. In addition, participants reported increased reactivity, including drug craving, when presented with personalized trauma imagery cues. This is the first study to demonstrate increased drug craving in response to trauma cues in SUD–PTSD comorbid individuals.

In addition to demonstrating drug cue reactivity in SUD–PTSD comorbidity, this study demonstrated significant differences in cue reactivity between CD and AD comorbid individuals. Specifically, the AD group reported significantly higher drug craving, approach, and arousal, and lower avoidance ratings in response to the imagery and *in vivo* cues than the CD group, and the AD group reported significantly lower dominance ratings in response to the *in vivo* cues than the CD group. AD and CD groups differed in their response to the imagery cues despite similar vividness ratings. To our knowledge, no other study has directly

compared cue reactivity in CD and AD samples.

To elucidate the differences in CD and AD reactivity, the two groups were analyzed based on the inclusion of substance use, intoxication, or involvement within the personalized trauma script (e.g., the assailant was intoxicated, the victim was intoxicated, trauma occurred during the acquisition of illicit drugs). The drug content within the AD participants' trauma script did not impact their ratings of the imagery cues or their ratings of the *in vivo* cues. In contrast, the CD participants with drug content in their personalized trauma scripts (Drug+) reported significantly higher craving and approach in response to the imagery cues as compared to participants without drug content in their trauma scripts (Drug-). The CD Drug+ participants also reported less positive emotion and higher craving and approach ratings in response to the *in vivo* cues than the CD Drug- participants. One possible explanation for the increased reactivity within the Drug+ CD group comes from the nicotine literature. Tiffany and Drobes (1990) presented imagery scripts to smokers that were designed to elicit either negative, positive, or neutral affect and that contained either drug content (i.e. a description of a smoking situation) or no drug content (i.e., a description of a nonsmoking situation). Imagery scripts that contained drug content and elicited negative affect produced the highest drug craving among all of the affect-drug content combinations. Similarly for the CD group, trauma scripts that produced negative affect and included drug content elicited higher craving and approach ratings than did trauma cues that did not contain drug references. Therefore, it may be that the patients in the CD group were not responding to the negative emotional properties of the trauma script and instead were responding to the Drug+ scripts as a pure drug cue.

The striking differences in cue reactivity between the AD and CD groups were not expected. Based largely on clinical observations and patient reports of intense craving for cocaine, we expected that the CD group would have stronger cue reactions than the AD group in response to both drug and trauma cues. However, the AD group was more reactive to both types of cues despite the fact that the two groups did not differ on the number of days since their last use of their preferred substance.

The most direct explanation for our findings is that while the comorbidity of cocaine dependence and PTSD is relatively common (Back and Brady), cocaine dependent individuals with PTSD may not use cocaine to manage their PTSD symptoms as reliably as AD individuals. This possible differential drug use — PTSD symptom pairing may result in relatively weaker learned associations between PTSD symptoms and cocaine cues. These weaker learned associations would explain the relatively weaker drug-related responses elicited by the trauma cues in the CD group compared to the AD group. This is a logical explanation of our findings when the drug class and the disorder class are considered. PTSD is an anxiety disorder and cocaine is a powerful CNS stimulant. The stimulatory drug-effect from cocaine self administration (e.g. increased heart rate) may not be desirable when an individual with PTSD is experiencing PTSD symptoms (e.g. intrusive memories of the trauma). This undesirable stimulatory effect may result in relatively little cocaine use intended to modulate PTSD-induced negative affect and result in only a moderate association between cocaine and trauma cues. Conversely, the anxiolytic properties of alcohol may reduce the severity of PTSD symptoms and therefore, reinforce its use when an individual experiences trauma symptoms (cf. Stasiewicz and Maisto, 1993). This hypothesis is supported by a correlational study of drug use situations of cocaine and alcohol dependent individuals. Cannon and colleagues (1992) found that cocaine dependent males were less likely to use cocaine when experiencing negative emotion and males dependent on both cocaine and alcohol were more likely to use alcohol, rather than cocaine, when experiencing

negative emotion. However, our hypothesis remains speculative at this time since there is no empirical evidence that AD individuals pair alcohol consumption with PTSD symptoms to a greater degree than CD individuals pair cocaine consumption with PTSD symptoms.

In addition to differences between AD and CD groups' reactivity to the imagery cues, AD participants were significantly more reactive to the *in vivo* cues (i.e. alcohol and cocaine cues) than the CD participants. This result was also unexpected. Clinical lore and empirically-based reports of significant craving in CD individuals (e.g. Robbins and Ehrman, 1998), suggested to us that the CD group should report higher craving and other drug-related responses to the drug cues than the AD group. It is possible that the two groups differed in addiction severity or treatment motivation, variables that were not directly measured in the current study but could theoretically affect cue reactivity. As both groups met diagnostic criteria for substance dependence and were voluntarily involved in substance use treatment, it is unlikely that these variables could fully explain the differences found between the AD and CD groups. Another possible explanation is that the CD group did not believe that the simulated crack cocaine presented to them was authentic as they were told. This explanation is improbable since most CD participants were surprised to learn that the simulated cocaine was not authentic and, in fact, one participant could not be convinced that the cocaine cue was simulated. A more likely explanation may be that intense cocaine craving has a limited time course and that the current study's 4-day abstinence requirement may have placed participants well outside that window of peak craving. This hypothesis is supported by the research of Robbins and Ehrman (1998) who found that cocaine craving was higher during 2–3 day periods in which cocaine was used rather than prior to or following these periods of cocaine use. This hypothesis is further supported by studies of protracted cocaine withdrawal that report relatively low craving in cocaine using inpatients (Weddington and Satel) and cocaine dependent outpatients (Coffey et al., 2000).

Another possible contributing factor may have been the autonomic hyperarousal that occurs in both acute and protracted alcohol withdrawal but probably plays less of a role in cocaine withdrawal. While the alcohol group should not have been in acute withdrawal 4 days after last use, they were very likely to be in the protracted abstinence phase (Satel et al., 1993) which might explain their increased reactivity to stimuli of all kinds. Thus, the differences in pharmacological properties of these two agents and the differences in the abstinence syndrome produced by them may help to explain this differential reactivity.

It is important to note that while AD participants were more reactive to imagery and *in vivo* cues than their CD counterparts, this is not to say that CD participants were not significantly reactive to the cues. In fact, consistent with reports from other investigators examining cue reactivity in CD individuals, CD participants in the current study were significantly reactive to the drug cue when compared to the neutral cue. Furthermore, consistent with studies on other substances of increased drug craving in response to negative emotion (Childress; Cooney and Coffey) and consistent with reported increases in cocaine craving in response to induced psychological stress in cocaine abusers (Sinha et al., 1999), CD participants were more reactive to trauma cues than the neutral cues.

One limitation of the current study is the significant demographic differences between the CD and AD groups. These differences are consistent with demographic dissimilarities found in the alcohol and cocaine dependent populations in the Charleston, SC area and contribute to the ecological validity of our findings. Although it does not appear that these differences influenced reactivity to the cues, future studies should control for this potential source of variability. On the other hand, it is possible that differences between the CD and AD groups

on years of dependence (i.e. chronological age minus age of onset for substance dependence) may have influenced reactivity in the groups. However, this potential source of variance is quite difficult to assess for and control because different substances have different physiological, phenomenological, social, and economic effects on humans. For example, it is unlikely that the impact of 2 years of crack cocaine dependence is equivalent to the impact of 2 years of alcohol dependence. This differential impact of substance dependence may lead to quantitative and qualitative differences on the variable `years of dependence' so that a common metric does not truly exist. Moreover, the differences in the number of years the two groups are substance dependent is further confounded by the markedly different reinforcement values of crack cocaine and alcohol. Due to these largely unknown and uncontrollable differences, we believe that attempting to control for differences in years of dependence when comparing groups dependent on different substances may be misleading.

An important implication of the present findings is that SUD–PTSD comorbid individuals' poorer treatment outcome (Brady and Ouimette) may be directly related to their symptoms of PTSD, especially their intrusive symptoms. It is clear from our results that SUD patients react to personalized trauma-image cues with increased craving and other substance-related responses. It is also clear that personalized trauma-image cues that have drug cues imbedded within them significantly increase drug craving in CD patients. Whether CD individuals respond to the trauma cue as a negative emotion cue, as a `pure' drug cue, or as a combined negative emotion-drug cue, may be irrelevant since approximately two-thirds of our CD sample reported that their most horrific trauma was, in some way, drug-related and, consequently, increased drug craving. While the direct role of craving in substance use and relapse remains unclear (Tiffany and Carter, 1998), there is no denying its clinical importance.

Our results also underscore the role of negative emotion in cocaine and alcohol dependence and suggest that this role may not be uniform across substances of abuse and substance abusers. In this study, a relatively weaker responsivity to negative emotional cues in CD individuals compared to AD individuals was demonstrated. This finding is consistent with Cannon et al. (1992) and suggests that the role of positive emotion in maintaining cocaine dependence may be relatively more important in CD individuals than the role of negative emotion. If this finding is supported by future research, treatments for cocaine dependence may be improved by developing strategies to help patients experience both positive and negative emotions without the aid of cocaine. Future studies of CD should address this potentially important variable.

Perhaps the most important implication of this study is to underscore the importance of treating both substance dependence and PTSD when they co-occur. Numerous researchers have documented the poorer substance abuse treatment outcome of SUD–PTSD comorbid individuals and have recommended concurrent treatment for the two disorders (Najavits; Ouimette; Triffleman and Coffey). The results from the current study provide experimental evidence that trauma-related imagery cues (i.e. memories) increase craving in individuals suffering from both PTSD and either alcohol or cocaine dependence. As trauma-related intrusive memories are a core diagnostic feature of PTSD, it is reasonable to assume that intrusive symptoms of PTSD may play a significant role in the maintenance of drug dependence in SUD–PTSD comorbid individuals and therefore should be addressed in substance use treatment.

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Alcohol Withdrawal Syndrome

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The spectrum of alcohol withdrawal symptoms ranges from such minor symptoms as insomnia and tremulousness to severe complications such as withdrawal seizures and delirium tremens. Although the history and physical examination usually are sufficient to diagnose alcohol withdrawal syndrome, other conditions may present with similar symptoms. Most patients undergoing alcohol withdrawal can be treated safely and effectively as outpatients. Pharmacologic treatment involves the use of medications that are cross-tolerant with alcohol. Benzodiazepines, the agents of choice, may be administered on a fixed or symptom-triggered schedule. Carbamazepine is an appropriate alternative to a benzodiazepine in the outpatient treatment of patients with mild to moderate alcohol withdrawal symptoms. Medications such as haloperidol, beta blockers, clonidine, and phenytoin may be used as adjuncts to a benzodiazepine in the treatment of complications of withdrawal. Treatment of alcohol withdrawal should be followed by treatment for alcohol dependence. (Am Fam Physician 2004;69:1443-50. Copyright© 2004 American Academy of Family Physicians)

See page 1339 for definitions of strength-of-recommendation labels.

In 1992, approximately 13.8 million Americans (7.4 percent of the U.S. adult population)[1] met the criteria for alcohol abuse or dependence as specified in the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, text revision (DSM-IV-TR).[2] In 2000, 226,000 patients were discharged from short-stay hospitals (excluding Veteran's Affairs and other federal hospitals) with one of the following diagnoses: alcohol withdrawal *(Table 1)*,[2] alcohol withdrawal delirium, or alcohol withdrawal hallucinosis.[3] It is estimated that only 10 to 20 percent of patients undergoing alcohol withdrawal are treated as inpatients,[4] so it is possible that as many as 2 million Americans may experience symptoms of alcohol withdrawal conditions each year.

Pathophysiology

Alcohol withdrawal syndrome is mediated by a variety of mechanisms. The brain maintains neurochemical balance through inhibitory and

excitatory neurotransmitters. The main inhibitory neurotransmitter is gamma-aminobutyric acid (GABA), which acts through the GABA-alpha (GABA-A) neuroreceptor. One of the major excitatory neurotransmitters is glutamate, which acts through the *N*-methyl-D-aspartate (NMDA) neuroreceptor.

Alcohol enhances the effect of GABA on GABA-A neuroreceptors, resulting in decreased overall brain excitability. Chronic exposure to alcohol results in a compensatory decrease of GABA-A neuroreceptor response to GABA, evidenced by increasing tolerance of the effects of alcohol.

Alcohol inhibits NMDA neuroreceptors, and chronic alcohol exposure results in up-regulation of these receptors. Abrupt cessation of alcohol exposure results in brain hyperexcitability, because receptors previously inhibited by alcohol are no longer inhibited. Brain hyperexcitability manifests clinically as anxiety, irritability, agitation, and tremors. Severe manifestations include alcohol withdrawal seizures and delirium tremens.

An important concept in both alcohol craving and alcohol withdrawal is the "kindling" phenomenon; the term refers to long-term changes that occur in neurons after repeated detoxifications. Recurrent detoxifications are postulated to increase obsessive thoughts or alcohol craving.[5] Kindling explains the observation that subsequent episodes of alcohol withdrawal tend to progressively worsen.

Although the significance of kindling in alcohol withdrawal is debated, this phenomenon may be important in the selection of medications to treat withdrawal. If certain medications decrease the kindling effect, they may become preferred agents.

TABLE 1
Diagnostic Criteria for Alcohol Withdrawal

A. Cessation of (or reduction in) alcohol use that has been heavy and prolonged.
B. Two (or more) of the following, developing within several hours to a few days after criterion A:
   1. Autonomic hyperactivity (e.g., sweating or pulse rate greater than 100 beats per minute)
   2. Increased hand tremor
   3. Insomnia
   4. Nausea or vomiting
   5. Transient visual, tactile, or auditory hallucinations or illusions
   6. Psychomotor agitation
   7. Anxiety
   8. Grand mal seizures
C. The symptoms in criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Adapted with permission from American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed., text revision. Washington, D.C.: American Psychiatric Association, 2000:216.

Withdrawal Symptoms

The spectrum of withdrawal symptoms and the time range for the appearance of these symptoms after cessation of alcohol use are listed in *Table 2*. Generally, the symptoms of alcohol withdrawal relate proportionately to the amount of alcoholic intake and the duration of a patient's recent drinking habit. Most patients have a similar spectrum of symptoms with each episode of alcohol withdrawal.

TABLE 2
Symptoms of Alcohol Withdrawal Syndrome

Symptoms	*Time of appearance after cessation of alcohol use*
Minor withdrawal symptoms: insomnia, tremulousness, mild anxiety, gastrointestinal upset, headache, diaphoresis, palpitations, anorexia	6 to 12 hours
Alcoholic hallucinosis: visual, auditory, or tactile hallucinations	12 to 24 hours*
Withdrawal seizures: generalized tonic-clonic seizures	24 to 48 hours†
Alcohol withdrawal delirium (delirium tremens): hallucinations (predominately visual), disorientation, tachycardia, hypertension, low-grade fever, agitation, diaphoresis	48 to 72 hours‡

*—*Symptoms generally resolve within 48 hours.*
†—*Symptoms reported as early as two hours after cessation.*
‡—*Symptoms peak at five days.*

Minor withdrawal symptoms can occur while the patient still has a measurable blood alcohol level. These symptoms may include insomnia, mild anxiety, and tremulousness. Patients with alcoholic hallucinosis experience visual, auditory, or tactile hallucinations but otherwise have a clear sensorium.

Withdrawal seizures are more common in patients who have a history of multiple episodes of detoxification. Causes other than alcohol withdrawal should be considered if seizures are focal, if there is no definite history of recent abstinence from drinking, if seizures occur more than 48 hours after the patient's last drink, or if the patient has a history of fever or trauma.

Alcohol withdrawal delirium, or delirium tremens, is characterized by clouding of consciousness and delirium. Episodes of delirium tremens have a mortality rate of 1 to 5 percent.[6] Risk factors for developing alcohol withdrawal delirium include concurrent acute medical illness, daily heavy alcohol use, history of delirium tremens or withdrawal seizures, older age, abnormal liver function, and more severe withdrawal symptoms on presentation.

Evaluation of the Patient in Alcohol Withdrawal

The history and physical examination establish the diagnosis and severity of alcohol withdrawal. Important historical data include quantity of alcoholic intake, duration of alcohol use, time since last drink, previous alcohol withdrawals, presence of concurrent medical or psychiatric conditions, and abuse of other agents. In addition to identifying withdrawal symptoms, the physical examination should assess possible complicating medical conditions, including arrhythmias, congestive heart failure, coronary artery disease, gastrointestinal bleeding, infections, liver disease, nervous system impairment, and pancreatitis. Basic laboratory investigations include a complete blood count, liver function tests, a urine drug screen, and determination of blood alcohol and electrolyte levels.

The revised Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scale is a validated 10-item assessment tool that can be used to quantify the severity of alcohol withdrawal syndrome, and to monitor and medicate patients going through withdrawal[7,8] *(Figure 1)*.[7] CIWA-Ar scores of 8 points or fewer correspond to mild withdrawal, scores of 9 to 15 points correspond to moderate withdrawal, and scores of greater than 15 points correspond to severe withdrawal symptoms and an increased risk of delirium tremens and seizures.

Assessment of Alcohol Withdrawal

Patient: _____ Date: _____ Time: _____

Pulse or heart rate, taken for one minute: _____ Blood pressure: _____/_____

Nausea and vomiting. Ask "Do you feel sick to your stomach? Have you vomited?"

Observation:

0—No nausea and no vomiting
1—Mild nausea with no vomiting
2—
3—
4—Intermittent nausea with dry heaves
5—
6—
7—Constant nausea, frequent dry heaves, and vomiting

Tremor. Ask patient to extend arms and spread fingers apart.

Observation:

0—No tremor
1—Tremor not visible but can be felt fingertip to fingertip
2—
3—
4—Moderate tremor with arms extended
5—
6—
7—Severe tremor, even with arms not extended

Paroxysmal sweats

Observation:

0—No sweat visible
1—Barely perceptible sweating; palms moist
2—
3—
4—Beads of sweat obvious on forehead
5—
6—
7—Drenching sweats

Anxiety. Ask "Do you feel nervous?"

Observation:

0—No anxiety (at ease)
1—Mildly anxious
2—
3—
4—Moderately anxious or guarded, so anxiety is inferred
5—
6—
7—Equivalent to acute panic states as occur in severe delirium or acute schizophrenic reactions

Agitation

Observation:

0—Normal activity
1—Somewhat more than normal activity
2—
3—
4—Moderately fidgety and restless
5—
6—
7—Paces back and forth during most of the interview or constantly thrashes about

Tactile disturbances. Ask "Do you have you any itching, pins-and-needles sensations, burning, or numbness, or do you feel like bugs are crawling on or under your skin?"

Observation:

0—None
1—Very mild itching, pins-and-needles sensation, burning, or numbness
2—Mild itching, pins-and-needles sensation, burning, or numbness
3—Moderate itching, pins-and-needles sensation, burning, or numbness
4—Moderately severe hallucinations
5—Severe hallucinations
6—Extremely severe hallucinations
7—Continuous hallucinations

Auditory disturbances. Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?"

Observation:

0—Not present
1—Very mild harshness or ability to frighten
2—Mild harshness or ability to frighten
3—Moderate harshness or ability to frighten
4—Moderately severe hallucinations
5—Severe hallucinations
6—Extremely severe hallucinations
7—Continuous hallucinations

Visual disturbances. Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?"

Observation:

0—Not present
1—Very mild sensitivity
2—Mild sensitivity
3—Moderate sensitivity
4—Moderately severe hallucinations
5—Severe hallucinations
6—Extremely severe hallucinations
7—Continuous hallucinations

Headache, fullness in head. Ask "Does your head feel different? Does it feel like there is a band around your head?"

Do not rate for dizziness or lightheadedness; otherwise, rate severity.

0—Not present
1—Very mild
2—Mild
3—Moderate
4—Moderately severe
5—Severe
6—Very severe
7—Extremely severe

Orientation and clouding of sensorium. Ask "What day is this? Where are you? Who am I?"

Observation:

0—Oriented and can do serial additions
1—Cannot do serial additions or is uncertain about date
2—Date disorientation by no more than two calendar days
3—Date disorientation by more than two calendar days
4—Disoriented for place and/or person

Total score: _____ (maximum = 67) Rater's initials: _____

FIGURE 1. Revised Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scale.

Adapted from Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of

alcohol withdrawal: the revised Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA-Ar). Br J Addict 1989;84:1353-7.

In using the CIWA-Ar, the clinical picture should be considered because medical and psychiatric conditions may mimic alcohol withdrawal symptoms. In addition, certain medications (e.g., beta blockers) may blunt the manifestation of these symptoms.

Differential Diagnosis

Alcohol withdrawal syndrome can be confused with other conditions. Thyrotoxicosis, anticholinergic drug poisoning, and amphetamine or cocaine use can result in signs of increased sympathetic activity and altered mental status. Central nervous system infection or hemorrhage can cause seizures and mental status changes. Withdrawal from other sedative-hypnotic agents causes symptoms similar to those occurring in alcohol withdrawal syndrome.

Goals of Treatment

The American Society of Addiction Medicine lists three immediate goals for detoxification of alcohol and other substances: (1) "to provide a safe withdrawal from the drug(s) of dependence and enable the patient to become drug-free"; (2) "to provide a withdrawal that is humane and thus protects the patient's dignity"; and (3) "to prepare the patient for ongoing treatment of his or her dependence on alcohol or other drugs."[6]

General Care

Abnormalities in fluid levels, electrolyte levels, or nutrition should be corrected. Intravenous fluids may be necessary in patients with severe withdrawal because of excessive fluid loss through hyperthermia, sweating, and vomiting. Intravenous fluids should not be administered routinely in patients with less severe withdrawal, because these patients may become overhydrated.

Routine administration of magnesium sulfate has not been shown to improve withdrawal symptoms,[9] but supplementation is appropriate if a patient is hypomagnesemic. Multivitamins and thiamine (100 mg per day) should be provided during treatment for alcohol withdrawal. If intravenous fluids are administered, thiamine (100 mg intravenously) should be given before glucose is administered, to prevent precipitation of Wernicke's encephalopathy.

Medication Regimens

Medication can be administered using fixed-schedule or symptom-triggered regimens *(Table 3).*[10] With a fixed-schedule regimen, doses of a benzodiazepine are administered at specific intervals, and additional doses of the medication are given as needed based on the severity of the withdrawal symptoms. In a symptom-triggered regimen, medication is given only when the CIWA-Ar score is higher than 8 points.

TABLE 3

Examples of Treatment Regimens for Alcohol Withdrawal

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Symptom-triggered regimens have been shown to result in the administration of less total medication and to require a shorter duration of treatment.[11,12] In one randomized, double-blind controlled trial,[11] patients in the symptom-triggered group received an average of 100 mg of chlordiazepoxide, whereas patients in the fixed-schedule group received an average of 425 mg. The median duration of treatment in the symptom-triggered group was nine hours, compared with 68 hours in the fixed-schedule group. Patients were excluded from the study if they had concurrent medical or psychiatric illness requiring hospitalization or seizures from any cause.[11]

Another trial[12] yielded similar results, with patients in the fixed-schedule group receiving an average of 231.4 mg of oxazepam and those in the symptom-triggered group receiving an average of 37.5 mg. Of the patients in the symptom-triggered group, 61 percent did not receive any oxazepam. This trial excluded persons with major psychiatric, cognitive, or medical comorbidities.

The use of symptom-triggered therapy requires training of the clinical staff. If this training has not been provided, fixed-schedule pharmacotherapy should be used.[10]

Choice of Treatment Setting

In most patients with mild to moderate withdrawal symptoms, outpatient detoxification is safe and effective, and costs less than inpatient treatment.[4,13-15] However, certain patients should be considered for inpatient treatment regardless of the severity of their symptoms. Relative indications for inpatient alcohol detoxification are as follows: history of severe withdrawal symptoms, history of withdrawal seizures or delirium tremens, multiple previous detoxifications, concomitant psychiatric or medical illness, recent high levels of alcohol consumption, pregnancy, and lack of a reliable support network.[16]

In most patients with mild to moderate withdrawal symptoms, outpatient detoxification is safe and effective, and costs less than inpatient treatment.

If outpatient treatment is chosen, the patient should be assessed daily. The patient and support person(s) should be instructed about how to take the withdrawal medication, the side effects of the medication, the expected withdrawal symptoms, and what to do if symptoms worsen.[6,17] Small quantities of the withdrawal medication should be prescribed at each visit; thiamine and a multivitamin also should be prescribed. Because close monitoring is not available in ambulatory treatment, a fixed-schedule regimen should be used.

Pharmacologic Treatment of Withdrawal

BENZODIAZEPINES

Pharmacologic treatment of alcohol withdrawal syndrome involves the use of medications that are cross-
tolerant with alcohol. Benzodiazepines have been shown to be safe and effective, particularly for preventing or treating seizures and delirium, and are the preferred agents for treating the symptoms of alcohol withdrawal
syndrome.[10]

The choice of agent is based on pharmacokinetics. Diazepam (Valium) and chlordiazepoxide (Librium) are long-acting agents that have been shown to be excellent in treating alcohol withdrawal symptoms. Because of the long half-life of these medications, withdrawal is smoother, and rebound withdrawal symptoms are less likely to occur. Lorazepam (Ativan) and oxazepam (Serax) are intermediate-acting medications with excellent records of efficacy. Treatment with these agents may be preferable in patients who metabolize medications less effectively, particularly the elderly and those with liver failure. Lorazepam is the only benzodiazepine with predictable intramuscular absorption (if intramuscular administration is necessary).

Rarely, it is necessary to use extremely high dosages of benzodiazepines to control the symptoms of alcohol withdrawal. Dosages of diazepam as high as 2,000 mg per day have been administered.[18] Because clinicians often are reluctant to administer exceptionally high dosages, undertreatment of alcohol withdrawal is a common problem.

One randomized controlled trial (RCT)[19] affirmed previous findings that carbamazepine is an effective alternative to benzodiazepines in the treatment of alcohol withdrawal syndrome in patients with mild to moderate symptoms. Patients in the study received 800 mg of carbamazepine on the first day, with the dosage tapered to 200 mg by the fifth day. Carbamazepine (Tegretol) also appears to decrease the craving for alcohol after withdrawal. It is not sedating and has little potential for abuse. Although carbamazepine is used extensively in Europe, its use in the United States has been limited by lack of sufficient evidence that it prevents seizures and delirium.

ADJUNCTIVE AGENTS

Several medications may be helpful adjuncts to benzodiazepines in the treatment of alcohol withdrawal syndrome. However, these medications should not be used as monotherapy.

Haloperidol (Haldol) can be used to treat agitation and hallucinations, although it can lower the seizure threshold. The use of atenolol (Tenormin) in conjunction with oxazepam has been shown to improve vital signs more quickly and to reduce alcohol craving more effectively than the use of oxazepam alone.[20]

Adjunctive treatment with a beta blocker should be considered in patients with coronary artery disease, who may not tolerate the strain that alcohol withdrawal can place on the cardiovascular system. Clonidine (Catapres) also has been shown to improve the autonomic symptoms of withdrawal.[10] Although phenytoin (Dilantin) does not treat withdrawal seizures, it is an appropriate adjunct in patients with an underlying seizure disorder.

Patient Follow-Up

Treatment of alcohol withdrawal syndrome should be followed by treatment for alcohol dependence. Treatment of withdrawal alone does not address the underlying disease of addiction and therefore offers little hope for long-term abstinence.

In the outpatient setting, brief interventions are helpful in patients with alcohol abuse,[21] but more

intense interventions are required in patients with alcohol dependence. The anticonvulsant topiramate (Topamax) has been shown to be an effective adjunctive medication to decrease alcohol consumption and increase abstinence in alcohol-dependent patients.[22]

Some patients achieve dramatic results by joining 12-step groups such as Alcoholics Anonymous and Narcotics Anonymous. Other patients benefit from stays in comprehensive treatment facilities, which offer a combination of a 12-step model, cognitive-behavior therapy, and family therapy. The treatment of alcohol withdrawal syndrome should be supplemented by an individualized, comprehensive treatment program, or at least as many elements of such a program as the patient can tolerate and afford.

Strength of Recommendations

Key clinical recommendation	*Strength of recommendation*	*References*
The revised Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scale is a validated 10-item assessment tool that can be used to quantify the severity of alcohol withdrawal syndrome, and to monitor and medicate patients going through withdrawal.	A	7,8
Symptom-triggered regimens have been shown to result in the administration of less total medication and to require a shorter duration of treatment.	A	11, 12
In most patients with mild to moderate withdrawal symptoms, outpatient detoxification is safe and effective, and costs less than inpatient treatment.	A	4, 13, 14, 15
Benzodiazepines have been shown to be safe and effective, particularly for preventing or treating seizures and delirium, and are the preferred agents for treating the symptoms of alcohol withdrawal syndrome.	A	10

Future Directions

Several medications have shown early promise in the treatment of alcohol withdrawal. In one case report[23] involving five patients, a single 10-mg dose of baclofen resulted in relief of severe withdrawal symptoms. In a preliminary RCT,[24] baclofen also reduced craving in alcohol-dependent patients.

Gabapentin, which is structurally similar to GABA, has been effective in the treatment of alcohol withdrawal in small studies.[25,26] The low toxicity of gabapentin makes it a promising agent. In another study,[27] the anticonvulsant agent vigabatrin, which irreversibly blocks GABA transaminase, improved withdrawal symptoms after only three days of treatment.

Prevention

Early identification of problem drinking allows prevention or treatment of complications, including severe withdrawal. The U.S. Preventive Services Task Force[28] recommends screening patients for problem drinking through a careful history or standardized screening questionnaire. Patients

undergoing preoperative evaluation also should be screened, because alcohol withdrawal can complicate recovery from surgery.[29] Elective surgery should be postponed until the dependent patient has not had alcohol for seven to 10 days.

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